Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research

To:	BLA 125587/70, Prior Approval Supplement – Efficacy Supplement
From:	Evi Struble, Ph.D., Research Pharmacology, PDB, DPPT, OTAT
Through:	Dorothy Scott, MD, Branch Chief, PDB, DPPT, OTAT
Applicant:	Octapharma
Product:	PANZYGA® (Immune Globulin Intravenous, human ifas 10%)
Subject:	Pharm/Tox Review

Contents

Introduction

Panzyga is a 10% Immune Globulin Intravenous preparation approved in 2018 for the indications of Primary Immunodeficiency and Chronic Immune Thrombocytopenia. With this submission, the sponsor seeks approval for Panzyga when used for Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) indication. Approved and sought doses for these indications are shown in Table 1.

Table 1: Dosage and Administration

Indication	Dose	Initial Infusion Rate	Maximum Infusion Rate (as tolerated)
PI	300-600 mg/kg (3-6 mL/kg) every 3-4 weeks	1 mg/kg/min (0.01 mL/kg/min)	14 mg/kg/min (0.14 mL/kg/min)
Chronic ITP in adults	1 g/kg (10 mL/kg) daily for 2 consecutive days	1 mg/kg/min (0.01 mL/kg/min)	8 mg/kg/min (0.08 mL/kg/min)

Indication	Dose	Initial Infusion Rate	Maximum Infusion Rate (as tolerated)
CIDP in adults	Loading dose: 2 g/kg (20 mL/kg), divided into 2 daily doses of 1 g/kg (10 mL/kg) given on 2 consecutive days Maintenance dose: 1 - 2 g/kg (10 - 20 mL/kg) every 3 weeks. Dose should be individualized.	1 mg/kg/min (0.01 mL/kg/min)	12 mg/kg/min (0.12 mL/kg/min)

Pharmacology and Toxicology

Nonclinical Studies, Main Findings

There were no new nonclinical studies submitted with this efficacy supplement. Nonclinical studies submitted in support of the original BLA were referenced. The main findings, as they relate to the sought indication are listed.

1. In single dose toxicity study in mice a preclinical preparation of Panzyga did not cause dose-dependent toxicity when administered at doses up to 5 times higher than a single dose of 2 g/kg. There were dose independent findings such as spleen and lymph node enlargement, sometimes associated with red discoloration. These findings could be related to the host immune response to the human biologic.
2. In single dose toxicity study in rats, a dose of a preclinical preparation equal to the total 2 g/kg was tolerated. The only toxicities noted were unqualified lung discolorations. Similar findings were also seen in vehicle and in saline controls.
3. There was no thrombogenic activity of clinical or preclinical preparations of Panzyga in the Wessler rabbit model when dosed at 1 g/kg, equal to the one-day dose (half of the total dose) for CIDP.
4. A nonclinical preparation of Panzyga caused no effects in blood pressure in spontaneously hypertensive rats or bronchiospastic effects in guinea pigs at doses similar to human dose.
5. There was no local toxicity in rabbits when 10 mL Panzyga was injected intravenously.

These studies support the approval of Panzyga for the CIDP indication.

Formulation and Impurities

Select product characteristics for Panzyga are shown in Table 2; they are not different from the marketed Panzyga product. The formulation and impurity profile for Panzyga when used for the CIDP indication, do not raise toxicologic concerns.

Table 2: Panzyga, Select Specifications

Ingredients	Concentration	Function
Total protein	(b) (4) mg/ml	

Immunoglobulins	(b) (4) 96% of total protein	Active ingredient
pH	4.5-5.0	
Glycine	15.0 – 19.5 mg/ml	(b) (4)
(b) (4)	(b) (4)	(b) (4)
Octoxynol (Triton X-100)	(b) (4)	Detergent, Impurity
TNBP	(b) (4)	Solvent, Impurity

Conclusions

There are no pharmacology/toxicology issues that would prevent this PAS from being approved.